



1400/0110

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

6/6/01
6/6/01

In re Application of Green et al.)
Art Unit: N/A)
Serial Number 09/823,992) Examiner: N/A)
Filed APRIL 3, 2001) Atty Ref: GRE001)

For: MASS SPECTROMETRY AND METHODS OF MASS SPECTROMETRY

THE COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

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Respectfully submitted,

Everett G. Diederiks, Jr.

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Attorney for Applicant
Registration Number: 33,323

Date: May 10, 2001



INVESTOR IN PEOPLE

The Patent Office
Concept House
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Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

1. Your reference	85.74495		
2. Patent application number (The Patent Office will fill in this part)	0029040.3		
3. Full name, address and postcode of the or of each applicant (underline all surnames)	Micromass Limited Floats Road, Wythenshawe Manchester, M23 9LZ United Kingdom		
Patents ADP number (if you know it)	06996102001		
If the applicant is a corporate body, give country/state of incorporation	United Kingdom		
4. Title of the invention	Orthogonal Time of Flight Mass Spectrometer		
5. Name of your agent (if you have one)	Frank B. Dehn & Co.		
"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)	179 Queen Victoria Street London EC4V 4EL		
Patents ADP number (if you know it)	166001		
6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number	Country	Priority application number (if you know it)	Date of filing (day / month / year)
7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application	Number of earlier application		Date of filing (day / month / year)
8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if: a) any applicant named in part 3 is not an inventor, or b) there is an inventor who is not named as an applicant, or c) any named applicant is a corporate body. See note (d))	Yes		

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9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form

Description

2/82

Claim(s)

Abstract

Drawing(s)

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

Request for preliminary examination and search (Patents Form 9/77)

Request for substantive examination (Patents Form 10/77)

Any other documents (please specify)

11.

I/We request the grant of a patent on the basis of this application.

Signature

Date 29 November 2000

12. Name and daytime telephone number of person to contact in the United Kingdom

P.M. Jeffrey
01273 244200

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Increasing Dynamic Range of an Orthogonal Time of Flight Mass Spectrometer Using Fast Sensitivity Switching During Acquisition.

Background.

TDC

The use of a time to digital converter (ion arrival counter) as an acquisition device for oaTOF results in a restriction to the ultimate dynamic range for the detection of short-lived signals. Even after the application of dead time correction software, ion signals resulting in more than 1 ion arrival, on average, per pushout event at a given m/z value, result in saturation, non linear response and inaccurate exact mass determination. This limitation is accentuated in GC MS applications because of the narrow chromatographic peaks presented to the TDC which can commonly be in the order of 2 seconds wide at the base. In this case, with the system operating at 25KHz pushout frequency, a total of 25,000 ions can be recorded for a given m/z value during a chromatographic peak elution before significant non linearity of response.

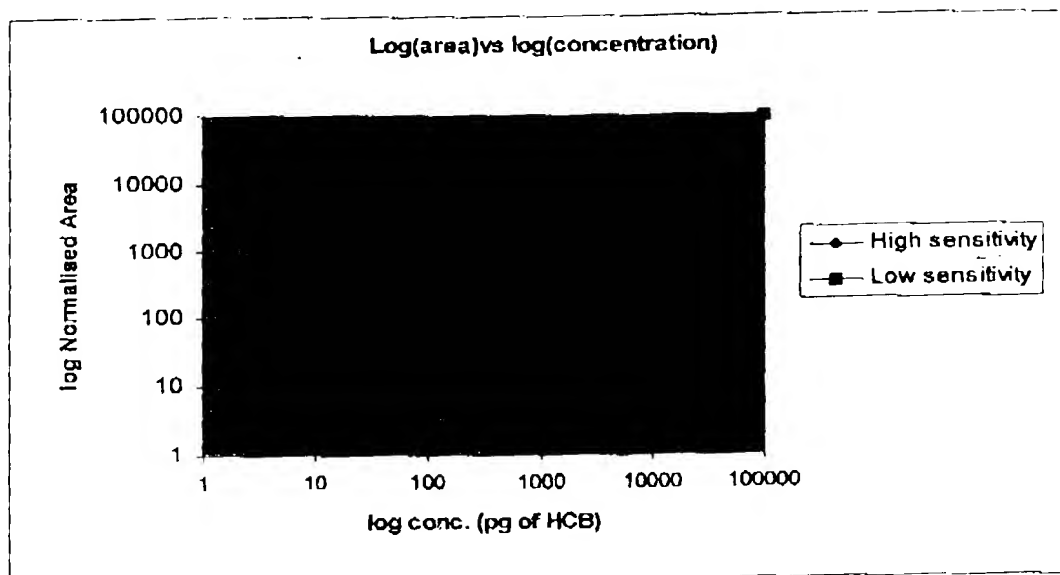
Principle of operation

To extend the dynamic range, the system has been designed to alternate between two sensitivity ranges during an acquisition. One range is tuned to be at high sensitivity. The second is adjusted to be at a lower sensitivity than the first by a factor of up to 100x. The two data streams are stored as two discrete functions presenting two discrete data sets. Once the ratio of the high sensitivity to low sensitivity data has been determined the data can be massaged to yield linear quantitative calibration curves over 4 orders of magnitude. Furthermore, the system can be arranged so that exact mass data can be extracted from either trace. Therefore, if a particular eluent produces a mass spectral peak which is saturated in the high sensitivity data set and therefore exhibits poor mass measurement accuracy, the same mass spectral peak may be unsaturated and correctly mass measured in the lower sensitivity trace. By using a combination of both traces, as sample elutes exact mass measurements may be produced over a wide range of sample concentration.

Description of design

A set of Z focussing lenses are installed into the outer ion source in a field free region of the optics. These are connected to a fast switching power supply capable of supplying from -100 to +100V DC. Initially the system is tuned to full sensitivity. The Z focusing lens voltage is then varied manually until the desired lower sensitivity is reached. Acquisition then results in fast switching of the Z lens power supply between two (or more) pre-determined voltages between each spectrum. Spectra are stored as separate functions to be post processed

Preliminary results



The graph above demonstrates four orders of magnitude dynamic range using a combination of data from both the high and low sensitivity data sets. The system was tuned to give a ratio of approx. 80:1 between the high and low sensitivity data sets. The experiment allowed equal acquisition time for both data sets alternating between the two sensitivity ranges between spectra.

Standard solutions ranging in concentration from 10 pg – 100ng of HCB were injected via the GC. The peak area response for the reconstructed ion chromatogram of m/z 283.8102 was plotted against the concentration. The results from the low sensitivity data set were multiplied by 80x before plotting, to normalise them to the high sensitivity data set.

Specific features

Exact mass measurement can be made using a single point lock mass common to both high and low sensitivity ranges.

Utilising Z focusing minimises any change in resolution, mass position and spectral skew associated with focussing/ deflection in the Y direction.

The relative dwell time for the high and low sensitivity functions can be varied. This will allow minimum sensitivity loss for the high sensitivity trace whilst still allowing the maximum increase in dynamic range.

This is the first time that this approach has been used with oaTOF technology.

At least 1 order of magnitude increase in dynamic range can be achieved, from 3.25 – 4.25 orders of magnitude.